International Journal of Hygiene and Environmental Health 215 (2012) 297–305

Contents lists available at SciVerse ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.de/ijheh

Childhood asthma and indoor allergen exposure and sensitization in Buffalo, New York

S. Lin [a,b], R. Jones [a,b,*], J.P. Munsie [a], S.G. Nayak [a], E.F. Fitzgerald [b], S.A. Hwang [a,b]

[a] Bureau of Environmental and Occupational Epidemiology, Center for Environmental Health, New York State Department of Health, Troy, NY 12180, United States
[b] University at Albany, SUNY, Department of Epidemiology and Biostatistics, School of Public Health, Rensselaer, NY 12144, United States

ARTICLE INFO

Article history:
Received 17 February 2011
Received in revised form 23 August 2011
Accepted 31 August 2011

Keywords:
Childhood asthma
Allergens
Allergen sensitization
Allergen exposure
Dust sampling
Indoor air

ABSTRACT

This nested case-control study examined the association between prevalent asthma and indoor allergen sensitization and/or exposure among children (aged 5–17 years) in Buffalo, New York. The study included a self-administered questionnaire, clinical interviews, skin allergen sensitivity tests and home dust sampling for house dust mites, cat, dog, cockroach and mouse allergens. After adjusting for multiple confounders, asthma cases had higher odds of being sensitized to *Der p* dust mites (odds ratio [OR] = 1.94, 95% confidence interval (CI): 1.13–3.35), cat (OR = 1.96, 95% CI: 1.13–3.39), or dog allergens (OR = 1.89, 95% CI: 1.10–3.22) than the controls. A significantly positive association between asthma status presence of cat allergen in the child's mattress (ORs: 2.61, 95% CI: 1.09–6.28) was also found. Children with both sensitization and environmental exposure to cat allergens had higher odds of asthma (OR = 7.08, 95% CI: 2.12–23.62) than those who were only sensitized to cat allergen (OR = 2.31, 95% CI: 1.01–5.32) or had only home exposures (OR = 1.47, 95% CI: 0.47–4.65). The association between allergen sensitization and asthma was more consistent than for home exposures. The findings help to confirm the role of allergen sensitization and home exposure in regard to asthma, and suggest that both, individually and jointly, are associated with asthma.

© 2011 Elsevier GmbH. All rights reserved.

Introduction

The prevalence of asthma in the United States has been increasing across all age groups since the 1980s, and is currently the most common chronic condition among children (Moorman et al., 2007). In 2005, the Centers for Disease Control and Prevention (CDC) reported an estimated 8.9% of children (6.5 million) in the U.S. currently had asthma (Bloom et al., 2006), while in 2003 there were 12.8 million school days missed by children (5–17 years) due to asthma (Bloom and Cohen, 2007). Previous studies have shown that residents in urban settings have higher rates of asthma (Aligne et al., 2000; Byrd and Joad, 2006; Mannino et al., 1998). One explanation for this phenomenon is that children in inner cities may be exposed to higher levels of various indoor allergens (Kitch et al., 2000) and may even be sensitized to these allergens at an early age (Call et al., 1992; Sarpong and Karrison, 1998). Several studies have found positive associations between asthma and sensitization to dust mite (Almqvist et al., 2007; Wong et al., 2002), cat (Chew, 2009), cockroach (Call et al., 1992) and mouse allergens (Phipatanakul et al., 2007). Many of these studies only evaluated atopic sensitization to a few specific allergens, rather than a panel of multiple allergens.

Exposure to indoor allergens in genetically susceptible children may be one mechanism leading to atopic sensitization (Arshad, 2010) and subsequently developed asthma (Gaffin and Phipatanakul, 2009). Several studies found asthma status to be significantly related to exposure to indoor environmental allergens, such as mouse allergen in U.S. households (Salo et al., 2009) or in urban elementary schools/homes (Sheehan et al., 2009). Other studies have linked detectable dust mite, cat, dog, or mouse allergens in the indoor environment to asthma (Brussee et al., 2005; Salo et al., 2008). However, some studies have not found significant associations between exposure to dust mite and cat allergens and asthma status (Lau et al., 2000; Surdu et al., 2006). Though the evidence for environmental exposures leading to sensitization is fairly consistent, as is the link between allergen sensitization and asthma risk, the role of environmental allergen exposures in the etiology of childhood asthma is less well-studied (Gaffin and Phipatanakul, 2009).

Another research gap pertains to the fact that most studies did not separate the effect of environmental exposure to allergens from that of sensitization on asthma. The few studies which have evaluated the joint effects of environmental exposure and sensitization to common allergens on asthma risk (Brussee et al., 2005; Gruchalla et al., 2005; Huss et al., 2001; Rosenstreich et al.,

* Corresponding author at: Center for Environmental Health, New York State Department of Health, Flanigan Square, Room 200, 547 River Street, Troy, NY 12180, United States. Tel.: +1 518 402 7989; fax: +1 518 402 7959.
E-mail address: rrj01@health.state.ny.us (R. Jones).

1438-4639/$ – see front matter © 2011 Elsevier GmbH. All rights reserved.
doi:10.1016/j.ijheh.2011.08.017

1997) relied on self-reported symptoms alone, and did not clinically confirm asthma status, or inadequately controlled for potential indoor and outdoor confounders. Furthermore, few research studies have examined relationships between allergen sensitization and exposure as well as between home characteristics and allergen exposure. To fill these research gaps, the primary objective of our study was to assess if asthmatic children were more likely to be sensitized or exposed (or both) to indoor allergens including animal (cat and dog) dander, cockroach, dust mite and mouse allergens, compared to non-asthmatic children after controlling for multiple risk factors. The secondary goals were to examine the relationship between sensitization and exposure, and to examine the relationship between self-reported home exposures and the presence of objectively measured allergens in the home.

Materials and methods

Study design and population

The current study is a nested case-control study conducted within a population-based cross-sectional study ($N = 3571$) that estimated the impact of indoor and outdoor environmental risk factors on asthma among children (1–17 years) living in the city of Buffalo, New York, the second most populous city in New York State. Methods used in the cross-sectional study (conducted in 1996) can be found in more detail in previously published papers (Jones et al., 2008; Lin et al., 2008). Procedures for the nested case-control study, including parent self-administered surveys, clinical interviews, skin allergen and home environment testing, were conducted among children (aged 5–17 years) living in Buffalo from 1999 to 2002.

Among all participants in the cross-sectional study who agreed to participate in possible follow-up, we generated a random subset of eligible cases and controls to recruit into the case-control study via telephone. Eligible cases were defined by the parent reporting at least two of the following seven criteria in the self-administered child health questionnaire during the cross-sectional study: current asthma; a physician diagnosis of asthma; ever wheezing; wheezing on most days or nights in past year; dry cough at night; exercise-related wheezing in the past year; and an emergency room or hospital visit due to asthma. We used these criteria for the following reasons: (1) to increase the validity of the case definition by using a combination of two asthma indicators; (2) to reduce potential misclassification of asthma status or reporting error by chance; (3) to capture all potential asthma cases rather than relying on physician diagnosis only. Children who did not report any of the criteria described above were defined as eligible controls, and a random sample of the eligible controls were then frequency-matched to cases by age (within 2 years), gender, and race. Children were excluded from eligibility if they reported any of the following: (1) a diagnosis of asthma prior to moving to their current residence; (2) living at their current residence for less than 1 year; and (3) non-cases that had been diagnosed with bronchitis or pneumonia in the past year.

Health survey

The two-part self-administered health questionnaire used in the cross-sectional study was adapted from the International Study of Asthma and Allergies in Childhood (Asher et al., 1995), the University of Sydney asthma questionnaire (Salome et al., 1987), and from the Second National Health and Nutrition Examination Survey (Crain et al., 1994). This questionnaire was validated via a pilot study within the same community. Part I of the survey comprised questions based on resident demographics, housing and lifestyle characteristics, and indoor and outdoor environmental exposures, while Part II comprised questions about the health and behavior of the index child (the eldest child in each participating home), including family history of asthma, asthma diagnosis, symptoms and severity, asthma triggers and the child's activity patterns.

Clinical assessment

Following phone recruitment and agreement to participate in the case-control study, the child's asthma status and symptoms were verified using questions from the cross-sectional survey instrument and clinically confirmed by a trained nurse or physician according to clinical criteria. Parents were additionally asked about the child's medical history, including a history of allergic rhinitis, eczema, sinusitis, allergies, medication use, asthma severity, smoking status and second hand smoke exposure. Information reported on allergies was used to decide whether the child could receive the allergen skin tests. Children who had taken corticosteroids or antihistamines in the past 72 hours or had a temperature of 37.8 °C or higher (which could affect the allergen testing results) were rescheduled for testing. Potential controls who were diagnosed with asthma during the clinical interview or who had a sibling diagnosed with asthma were considered ineligible to participate in the case-control study.

Skin allergen testing

Participants (84 cases and 109 controls) underwent skin allergen testing at Erie County Medical Center in Buffalo, New York to determine sensitivity to allergens: dust mites (*Der f* 1, *Der p* 1), cat (*Fel d* 1), dog (*Can f* 1), cockroach (*Bla g*1, *Bla g* 2), and mouse (mouse urinary protein, *MUP*). The tests were administered using the GREER®Pick® (Greer Laboratories, Inc.) following Dreborg's guidelines for skin testing (Dreborg, 1989). Prior to administering the allergens, histamine dihydrochloride (3 mg/ml) was administered as the positive control, since it almost universally causes an allergic response. Saline, a neutral substance, was administered as the negative control and also served to determine nonspecific skin reactivity. After 20 minutes of administering the allergen wheals and flares were measured using a digitalized graphics tablet developed with computer-aided design software (Jaen, 1996). The mean intra-tester and inter-tester coefficients of variation were low (3.1% and 2.9%), reflecting the high reliability of the testing protocol. Following repeated wheal measurements, a correlation coefficient of 0.97 (R^2) between wheal measurements was observed between individuals. Allergen sensitivity or atopy was defined as a positive reaction to an allergen where the diameter of the allergen wheal was larger than the saline wheal and at least 50% of the diameter of the histamine wheal (Dreborg, 1989; Paggiaro et al., 1986). Results for individuals with histamine wheals that were smaller than the saline wheal or less than 3 mm in diameter were excluded from the analysis.

Home environmental testing

Ninety-nine households that completed the questionnaire in the cross-sectional study and had the index child participating in the skin allergen testing and clinical interview were recruited for home environmental testing. As described in Appendix 1, the testing locations for collection of allergen samples included the family room, bedroom and kitchen (for a total of 9 allergens/locations). Specific allergens were selected for each location based on the allergens most common to these spaces. The allergens analyzed include dust mites (*Der p* 1 and *Der f* 1), cat (*Fel d* 1), dog (*Can f* 1), cockroach (*Bla g* 1 and *Bla g* 2), and mouse (Mouse Urinary Protein, *MUP*). Using a HEPA-filtered back-pack canister vacuum (Li'l Hummer®), trained project staff collected allergen samples by vacuuming each location for 2 minutes. If the sample appeared insufficient, vacuuming was continued for another 2 minutes. The sample was sifted using a brass number 50 mesh metal sieve

(Krackler Scientific) which excludes particles >300 μm, stored in a cooler, and sent to the Johns Hopkins University Dermatology, Allergy and Clinical Immunology (DACI) Reference Laboratory. Fine dust (100 mg) was then extracted overnight and evaluated by a panel of monoclonal antibody-based immunoenzymetric assays to quantify indicator molecules for the seven indoor aeroallergens for this study. Enzyme-Linked Immunosorbent Assays (ELISAs) were calibrated against national or international allergen standards as follows: World Health Organization (WHO) reference standard for *Der p* 1, *Der f* 1, and *Can f* 1; Center for Biologics Evaluation and Research (CBER) reference for *Fel d* 1; Indoor Biotechnologies standard for MUP, and the University of Virginia sub-standard for *Bla g* 1 and *Bla g* 2.

At least 5 mg of settled, sieved dust is required for allergen extraction and analysis (Platts-Mills, 1989). Information from previous studies (Platts-Mills, 1989) was used to define allergen threshold levels for development of sensitization/asthma. The thresholds used for this study were: dust mite (*Der p* 1 or *Der f* 1) levels greater than 10 μg/g; cat allergen (*Fel d* 1) levels greater than 8 μg/g; dog allergen (*Can f* 1) levels at or above the 75th percentile (>10 μg/g) since there was no threshold level available; and thresholds for cockroach (*Bla g* 1 *or Bla g* 2) and mouse (*MUP*) allergen was any level above the detection limit.

Informed consent was obtained from the parent or guardian of the child participants. All procedures were reviewed and approved by the Institutional Review Boards of the New York State Department of Health and the State University of New York (SUNY) at Buffalo.

Statistical analysis

An initial descriptive analysis was conducted to summarize the demographic distribution of the study participants. According to findings from our cross-sectional study (Lin et al., 2008), a total of five socio-demographic variables: gender, race, ethnicity, family history of asthma, and no time for medical care, and eight environmental factors: parent smoked, dampness in the home, humidifier use, chemical odor indoor or outdoor, cockroaches in house, frequent truck traffic in neighborhood and pets inside the house were examined as potential confounders. Since the population who underwent home environmental testing are a complete subset of those who had skin allergen testing, but also differed from the population of the cross-sectional study, we evaluated possible confounders separately for each group. Each of the respective models for skin allergen testing and home allergen exposure only included those variables significantly associated with asthma and with allergen exposure/sensitization in the controls in a bivariate analysis (Table 1).

Skin allergen test reactions in the participants were recorded for each allergen and compared between cases and controls. Because only a positive association was biologically plausible (i.e., effects in only one direction) and sample sizes were small, we used one-sided statistical tests to improve power. Crude and adjusted

Table 1
Asthma prevalence and socio-demographic and environmental factors for two study populations in Buffalo, New York.

Socio-demographic and home environmental factors	Home testing population			Skin allergen testing population		
	Cases (N = 50) N (%)	Controls (N = 49) N (%)	Crude OR[a] (95% CI)	Cases (N = 84) N (%)	Controls (N = 109) N (%)	Crude OR[a] (95% CI)
Gender						
Male	26 (52.0)	24 (48.9)	1.13 (0.58–2.19)	43 (8.3)	56 (51.4)	0.88 (0.55–1.42)
Female	24 (48.0)	25 (51.0)		46 (51.5)	53 (48.6)	
Race						
Black	5 (10.0)	6 (12.5)	0.78 (0.27–2.24)	11 (12.5)	25 (23.4)	0.47 (0.25–0.90)
All others	45 (90.0)	42 (87.5)		77 (87.5)	82 (76.64)	
Ethnicity						
Hispanic	0 (0.0)	7 (14.3)	–	5 (6.6)	17 (15.6)	0.32 (0.14–0.77)
Non-Hispanic	50 (100.0)	42 (85.7)		84 (94.4)	92 (84.4)	
Family history of asthma						
Yes	25 (50.0)	7 (14.3)	**6.00 (2.65–15.58)**	46 (51.7)	19 (17.4)	**5.07 (2.95–8.72)**
No	25 (50.0)	42 (85.7)		43 (48.3)	90 (82.6)	
No time for medical care						
Yes	2 (4.0)	0 (0.0)	–	2 (2.3)	3 (2.8)	0.79 (0.17–3.61)
No	48 (96.0)	49 (100.0)		87 (97.8)	103 (97.2)	
Either parent smoke						
Yes	14 (28.0)	17 (34.7)	0.73 (0.36–1.50)	34 (39.5)	36 (35.6)	1.18 (0.72–1.94)
No	36 (72.0)	32 (65.3)		52 (60.5)	65 (64.4)	
Dampness in house						
Yes	35 (71.4)	33 (68.8)	–	55 (62.5)	69 (65.7)	0.87 (0.53–1.43)
No	13 (28.6)	15 (31.3)		33 (37.5)	36 (34.3)	
Humidifier use						
Yes	26 (52.0)	23 (46.9)	1.22 (0.63–2.37)	46 (52.9)	43 (40.6)	**1.64 (1.02–2.66)**
No	24 (48.0)	15 (31.3)		41 (47.1)	63 (34.3)	
Chemical odor inside						
Yes	5 (10.0)	2 (4.1)	2.61 (0.63–10.78)	7 (7.9)	4 (3.7)	2.24 (0.78–6.46)
No	45 (90.0)	47 (95.9)		82 (92.1)	105 (96.3)	
Chemical odor outside						
Yes	15 (30.0)	10 (20.4)	1.67 (0.77–3.62)	26 (29.2)	20 (18.4)	**1.84 (1.05–3.21)**
No	35 (70.0)	39 (79.6)		63 (70.8)	89 (81.7)	
Cockroaches in the house						
Yes	1 (2.1)	2 (4.3)	0.48 (0.06–3.69)	1 (1.2)	5 (4.8)	0.24 (0.04–1.45)
No	47 (97.9)	45 (95.7)		85 (98.8)	100 (95.2)	
Frequent trucks passing						
Yes	23 (46.0)	15 (30.6)	1.93 (0.97–3.85)	40 (45.5)	35 (33.0)	**1.69 (1.04–2.76)**
No	27 (54.0)	34 (69.4)		48 (54.6)	71 (67.0)	
Pets inside the house						
Yes	30 (60.0)	25 (55.6)	1.20 (0.61–2.38)	47 (52.8)	52 (47.7)	1.23 (0.78–1.96)
No	20 (40.0)	20 (44.4)		42 (47.2)	57 (52.3)	

[a] Bold face OR (odds ratio) and CI (confidence interval) indicate significance at the α = 0.05 level.

odd ratios (OR) with 95% confidence intervals (CI) are presented using case-control status as the dependent variable. Indoor dust allergen levels were not normally distributed and were therefore compared between cases and controls using non-parametric tests.

For all analyses of the home environmental testing data as continuous variables, levels below the detection limit (<DL) were set to values of one-half of the detection limit reported by the laboratory. We defined the cut-point for analyses of multiple allergen exposure as the 75th percentile of the combined total number of locations where allergens were equal to or above the threshold, i.e., two possible locations for dust mites, cat, and dog respectively and one location for mouse after excluding cockroach allergen due to no exposed cases. Thus, the total number of allergens/locations above their thresholds ranged from 0 (minimum) to 7 (maximum), and the 75th percentile was 4 allergens/locations. The relationships between multiple allergens above the 75th percentile of thresholds and socio-demographic characteristics or various household factors were assessed. To examine sensitization related to exposure, we compared sensitization among children in households where allergens were measured to be greater to or equal to the threshold level for each allergen versus those below the threshold.

Results

Of the 202 children initially enrolled in the case-control study, we excluded four controls who had low baseline lung function measurements or reported asthma symptoms on the clinical questionnaire, four cases whose histamine wheal was less than or equal to the saline wheal, and one control who did not undergo skin allergen testing. All 193 of the remaining children (84 cases and 109 controls) were included in analyses, including 99 households (50 cases and 49 controls) who also agreed to participate in home environment sampling to test for the presence of allergens in indoor household dust.

Table 1 describes the relationships between asthma status and socio-demographics or environmental factors in two populations, one for skin allergen testing and another one for home allergen measurement. In the skin allergen testing group, we found that asthma was significantly associated with family history of asthma (OR = 5.07, 95% CI: 2.95–8.72), humidifier use (OR = 1.64, 95% CI: 1.02–2.66), chemical odor outside (OR = 1.84, 95% CI: 1.05–3.21) and frequent truck passing by the neighborhood (OR = 1.69, 95% CI: 1.04–2.76). These factors were considered as potential confounders and controlled in multivariate analyses in the population with skin allergen testing. Family history of asthma was the only variable related to asthma in the group with home allergen measurement, and was subsequently the only variable adjusted for in logistic regression analysis of this group.

Asthma and skin allergen testing

Median wheal size for saline was 3 mm among cases and 4 mm in the controls, while that for histamine was 7 mm in both cases and controls. Sensitization tests showed that reactions were significantly greater in the cases than in controls for both *Der p* dust mite (median 5 mm vs. 4 mm, $p < 0.05$) and cat allergen (median 5 mm vs. 4 mm, $p < 0.05$, data not shown).

Table 2 shows the number and percentage of cases and controls whose skin tests were positive for each allergen, along with crude and adjusted odds ratios and associated CIs. Prevalence of sensitization to dust mite, cat, and dog allergens was higher among cases than controls. After adjusting for potential confounders, including family members with asthma, chemical odors outdoors, humidifier use, and frequent neighborhood truck traffic, cases were significantly more likely to have a positive skin test for *Der p* dust mites (OR = 1.94, 95% CI: 1.13–3.35), cat (OR = 1.96, 95% CI: 1.13–3.39), and dog allergen (OR = 1.89, 95% CI: 1.10–3.22).

Asthma and allergen levels in home dust samples

Although the cases also seemed to have higher median levels of *Der f* 1 and *Der p* 1 dust mite and cat allergen than the controls, these differences were not statistically significant, possibly due to large variations in allergen levels between study homes (data not shown). Table 3 shows the relationship between indoor dust allergen levels and asthma case-control status. All 99 of the study homes had at least one allergen level above the detection limit and 25 homes had 4 or more allergens/locations above the threshold. Data for cockroach allergens are not presented since there were too few homes in this study with levels of cockroach allergen (*Bla g* 1 or *Bla g* 2) above the detection limit to conduct a statistical comparison, and there were no asthma cases with levels of cockroach allergen in the home above the detection limit. Forty-eight percent of the homes had dust mite allergen (*Der p* 1 and *Der f* 1 combined) above the threshold level, the greatest percentage among all of the allergens. All nine allergens/locations were above the threshold level in 9% of the study homes, and no homes had fewer than three allergens/locations above threshold level (data not shown). After controlling for the confounding effect of family members with asthma, cases were significantly more likely to have a cat allergen level above the threshold in their mattresses (OR = 2.61, 95% CI: 1.09–6.28). No other allergen nor home exposures to any allergen or multiple allergens/locations was significantly related to an increased odds of asthma.

As described in Table 4, multiple sources of allergen exposure at home (defined as allergens greater than the thresholds at 4 or more locations) was significantly associated with several

Table 2
Comparison of positive skin allergen tests between asthma cases ($N = 84$) and controls ($N = 109$).

Allergen	Positive skin allergen test[a]							
	Case		Control		Crude		Adjusted	
	N	%	*N*	%	OR[b]	95% CI	OR[c]	95% CI
Dust mites (*Der f* and *Der p*)	60	71.4	65	60.2	1.65	0.99–2.76	1.49	0.85–2.61
Der f dust mite	46	55.8	53	41.1	1.26	0.78–2.03	1.12	0.66–1.92
Der p dust mite	57	67.9	55	50.9	**2.03**	**1.24–3.35**	**1.94**	**1.13–3.35**
Cockroach	35	41.7	48	44.9	0.88	0.54–1.43	0.92	0.54–1.56
Cat	55	66.3	55	51.4	**1.86**	**1.13–3.05**	**1.96**	**1.13–3.39**
Dog	51	60.7	49	45.8	**1.83**	**1.12–2.98**	**1.89**	**1.10–3.22**
Mouse	39	45.9	51	47.7	0.93	0.58–1.50	1.13	0.66–1.94
Rat	35	41.7	44	41.5	1.01	0.62–1.64	0.90	0.52–1.57
Any one positive	78	91.8	100	92.6	0.89	0.37–2.16	1.02	0.38–2.75

[a] Positive if allergen wheal > saline wheal and at least 50% of histamine wheal.
[b] Bold face OR (odds ratio) and CI (confidence interval) indicate significance at the $\alpha = 0.05$ level.
[c] Adjusted for one or more family members with asthma, chemical odors outdoors, humidifier use, and frequent truck passing by.

Table 3
Multivariate logistic regression analysis of asthma and elevated levels of selected indoor allergens ($N=99$).

Allergen (threshold)[a]	Number above threshold	Cases		Adjusted OR[b]	95% CI
		Number	%		
Dust mite (*Der p* 1 ≥10 μg/g)					
in rug	9	5	10	0.59	0.16–2.23
in mattress	10	6	12	1.72	0.52–5.67
Dust mite (*Der f* 1 ≥10 μg/g)					
in rug	42	21	42	0.86	0.41–1.77
in mattress	40	19	38	0.72	0.35–1.51
Combined dust mite (*Der p* 1, *Der f* 1 ≥10 μg/g)					
in rug	48	25	50	1.11	0.54–2.28
in mattress	48	25	50	0.95	0.46–1.96
Cat (*Fel d* 1 ≥8 μg/g)					
in rug	26	16	32	2.11	0.92–4.83
in mattress	23	15	30	**2.61**	**1.09–6.28**
Dog (*Can f* 1 ≥10 μg/g)					
in rug	45	23	46	1.20	0.58–2.45
in mattress	32	17	34	1.13	0.53–2.43
Mouse in kitchen (*MUP* above detection limit)	21	8	16	0.45	0.18–1.14
Any allergen[c]	6	47	94	2.23	0.46–10.79
≥4 (75th percentile) locations with allergens	25	14	28	1.29	0.56–2.94

[a] Thresholds for dust mite and cat are based on previous studies. Since no previous studies were available for dog and mouse, dog threshold was set to the 75th percentile and mouse threshold was set at any level above the detection limit.
[b] Adjusted for one or more family members with asthma. Only one allergen was entered into each model. Bold face OR (odds ratio) and CI (confidence interval) indicate significance at the $\alpha=0.05$ level.
[c] Nine allergens/locations in the homes were tested for the presence of allergens; cockroach results have been excluded due to low detection limits.

Table 4
Relationship between related household factors and number of allergens/locations in study participants' homes ($N=99$).

Factor		Number of locations with allergens above the threshold[a]		
		≥4 locations (75th percentile)	Crude OR	95% CI
Cockroaches in house	Yes	1 (33.3)	1.15	0.19–11.69
	No	23 (25.0)	Ref	
Rats/mice in house	Yes	4 (50.0)	3.40	0.99–11.70
	No	20 (22.7)	Ref	
Home has carpet	Yes	24 (25.5)	0.69	0.09–5.34
	No	1 (33.3)	Ref	
Live in multiple-family house	Yes	7 (26.9)	1.06	0.45–2.50
	No	18 (25.7)	Ref	
Use humidifier	Yes	16 (32.7)	**2.21**	**1.01–4.85**
	No	9 (18.0)	Ref	
Any pet in house	Yes	23 (33.3)	**7.00**	**1.96–25.05**
	No	2 (6.7)	Ref	
Rodents in house	Yes	2 (15.4)	0.49	0.13–1.88
	No	23 (26.7)	Ref	
Presence of mold	Yes	7 (31.8)	1.63	0.67–3.96
	No	16 (22.2)	Ref	
Parent smoke in the house	Yes	9 (29.0)	1.33	0.60–2.97
	No	16 (23.5)	Ref	
Dampness in house	Yes	9 (31.0)	0.63	0.30–1.54
	No	15 (23.8)	Ref	
Stuffed animals in bedroom	Yes	15 (24.6)	0.91	0.42–1.99
	No	10 (26.3)	Ref	
Below poverty level	Yes	3 (25.00)	0.96	0.30–3.14
	No	19 (25.68)	Ref	
Mother's education	≤High school	7 (25.93)	1.01	0.43–2.38
	≥High school	17 (25.76)	Ref	
Marital status	Other	3 (17.65)	0.58	0.19–1.80
	Married	21 (26.92	Ref	
Child's gender	Male	15 (30.00)	1.67	0.77–3.62
	Female	10 (20.41)	Ref	
Child's age	5–17 years old	24 (25.53)	1.37	0.21–8.99
	0–4 years old	1 (20.00)	Ref	
Mother's race	Black	0 (0.00)	–	–
	All other	25 (28.74)	Ref	
Ethnicity	Hispanic	0 (0.00)	–	–
	All other	25 (25.17)	Ref	
Age of the house	>50 years	4 (26.67)	1.09	0.38–3.11
	≤50 years	21 (25.00)	Ref	

Bold face OR (odds ratio) and CI (confidence interval) indicate significance at the $\alpha=0.05$ level.
[a] The minimum and maximum number of locations with antigens above the threshold is 0 and 7, respectively.

Table 5
Sensitization to allergens among exposed and non-exposed children ($N = 99$).

Sensitized to specific allergens[a]	Increased allergen level in indoor dust (≥threshold)[b]		No increased allergen level indoors (<threshold)		Crude OR[c]	95% CI
	N	%	*N*	%		
Der f dust mite	31	52.5	17	50.0	1.11	0.55–2.25
Der p dust mite	9	64.3	44	55.7	1.43	0.53–3.85
Bla g 1 cockroach	4	80.0	34	38.6	**6.35**	**1.00–41.38**
Bla g 2 cockroach	3	75.0	35	39.3	4.63	0.67–31.97
Cat	15	57.7	30	45.5	1.64	0.76–3.53
Dog	23	51.1	26	54.2	0.88	0.45–1.75
Mouse	11	61.1	36	48.0	1.70	0.71–4.11

[a] Positive if allergen wheal > saline wheal and at least 50% of histamine wheal.
[b] Allergen levels were above their respective threshold levels.
[c] Bold face OR (odds ratio) and CI (confidence interval) indicate significance at the $\alpha = 0.05$ level.

home environmental factors, such as use of humidifier (OR = 2.21, 95% CI: 1.01–4.85) and having a pet in the house (OR = 7.00, 95% CI: 1.96–25.05). The households reporting having seen a rat or mouse were three times or more as likely to have multiple allergens/locations above the threshold, but this finding was not statistically significant.

Allergen sensitivity and allergen levels in home dust samples

To assess the relationship between environmental allergen exposure and allergen sensitization, children whose home had an elevated level of specific allergens (defined by exceeding the thresholds) were compared to those non-exposed (home dust allergens level < the threshold) to see if they were more likely to be sensitized to these specific allergens (Table 5). Although a higher percentage of children with home allergen exposure were more frequently sensitized to these specific allergens, with the exception of dog, the only borderline significant association was with *Bla g* 1 cockroach. Children exposed to *Bla g* 1 at home were about six times more likely to be sensitized to these cockroach allergens (OR = 6.35, 95% CI: 1.00–41.38) though the point estimate is imprecise due to the small sample size. Another interesting finding is that approximately 50% of the children without home allergen exposures were still sensitized to these allergens, with the exception of cockroach exposure.

Asthma, allergen sensitivity, and home allergen levels

Crude cat (*Fel d* 1) and dog (*Can f* 1), odds ratios for allergen presence and asthma were compared between children who were sensitized to the allergen, exposed to the allergen, or both (Table 6). While exposure without sensitization to any of the allergens was not significantlyassociated with asthma status, the analysis showed a higher odds of prevalent asthma for those who were sensitized but not exposed to cat allergens (OR = 2.31, 95% CI: 1.01–5.32) or to dog allergens (OR = 3.30, 95% CI: 1.22–8.94). Significant associations were also seen for the joint effect of sensitization and exposure to cat allergen, i.e., among those who were both sensitized and exposed to cat allergens (OR = 7.08, 95% CI: 2.12–23.62).

Discussion

Allergen sensitization and asthma

The current study showed significantly positive associations between asthma case-control status and sensitivity to cat, dog, and a dust mite (*Der p* 1) allergen. The odds of prevalent asthma increased by approximately 100% (OR = 1.94, 95% CI 1.13–3.35) for those who were sensitized to *Der p* 1 allergen, a finding which agrees with those from other studies examining the association between asthma and dust mite sensitization (Chew, 2009; Squillace et al., 1997). In the case-control study conducted by Squillace et al. (1997), sensitization to dust mite was associated with asthma in adolescents after controlling for confounding factors. Our study also found statistically significant associations between sensitization to cat allergen (OR = 2.02) and asthma, which is consistent with the findings of others (Sarpong and Karrison, 1997; Wong et al., 2002). Wong et al. (2002) found that among school children, sensitization to dust mite (Der *f* 1, OR = 3.67) and cat allergen (OR = 3.01), was significantly associated with bronchial hyper-responsiveness. Sarpong and Karrison (1997) found a similar, but a higher odds of prevalent asthma due to cat allergen sensitization (OR = 3.8, 95% CI: 1.5–9.2) than was observed our study (OR = 2.02, 95% CI: 1.16–3.51). In the current study, a positive association was found between asthma status and sensitization to dog allergens (OR = 1.99, 95% CI: 1.16–3.42), but this association was not observed in the Inner City Asthma Study (ICAS) by Gruchalla et al. (2005), which found a non-significant risk ratio for unscheduled asthma clinic visits among children sensitized to dog allergens (RR = 1.45, 95% CI: 0.98–2.14). The ICAS also found significant associations with cockroach allergen sensitization and clinic visits (RR = 1.40, 95% CI: 1.02–1.92). Several older case studies (Eggleston et al., 1998; Lindfors et al., 1999; Plaschke et al., 1999; Wilson et al., 1999) found a high prevalence of sensitization to various indoor allergens, as in our study, by skin prick testing or allergen specific IgE among asthma cases.

Table 6
Sensitization and/or indoor exposure to allergens and asthma[a] ($N = 99$).

Allergens	Sensitized and exposed		Exposed only		Sensitized only	
	Crude OR	95% CI OR	Crude OR	95% CI OR	Crude OR	95% CI OR
Dust mite	2.00	0.64–6.21	2.36	0.70–7.94	3.67	0.99–13.56
Cat	**7.08**	**2.12–23.62**	1.47	0.47–4.65	**2.31**	**1.01–5.32**
Dog	1.91	0.70–5.20	1.75	0.64–4.81	**3.30**	**1.22–8.94**
Mouse	0.29	0.08–1.00	1.03	0.26–4.03	0.86	0.40–1.85

Bold face OR (odds ratio) and CI (confidence interval) indicate significance at the $\alpha = 0.05$ level.
[a] The reference groups are those who were neither sensitized nor exposed to allergens in their home environment.

However, the sensitization-asthma association could not be assessed in these case studies since there were no comparison groups.

Home allergen exposure and asthma

Our analysis showed a significant association between prevalent asthma and cat allergen collected from mattresses (OR = 2.61, 95% CI: 1.09–6.28) after controlling for potential confounders, which is supported by other studies testing a similar hypothesis. Another nested case-control study in Germany (Gehring et al., 2001) reported a positive association between exposure to cat allergen and asthma symptoms among adults (OR = 2.74, 95% CI: 1.22–6.17). Similarly, a prospective cohort study led by Brussee et al. (2005) found borderline significant associations between persistent wheeze and exposure to cat among children (OR = 2.31, 95% CI: 0.98–5.46). Several studies support the plausibility of this relationship. A cross-sectional study by Plaschke et al. (1999) showed that living with a cat aggravated respiratory symptoms and inflammation biomarkers among 129 asthmatics sensitized to cat or dog allergen. Lindfors et al. (1999) found that exposure to cats is associated with sensitization to cat allergen in young asthmatic children in Sweden. Another study in Sweden (Almqvist et al., 2001) found that exposure to cat allergen can be encountered in the school environment, and asthma symptoms in children with cat allergy may worsen from indirect cat exposure at school.

Other studies have found associations between the severity of asthma symptoms and exposure to mouse (Salo et al., 2009; Sheehan et al., 2009) or house dust mite allergens (Michel et al., 1996). However, our study did not reveal a significantly greater level of mouse exposure among children with asthma, a finding consistent with a prospective birth cohort study in Germany (Lau et al., 2000) that assessed early mite and cat allergen exposures. Very few participating homes in our study had cockroach allergen levels above the detection level, which indicates that cockroach allergen may not be a major public health concern in the study area. Wide confidence intervals for several point estimates reflect the low precision for these findings. Finally, although the median concentration of the dust mite *Der p* 1 among cases in our study homes was low (0.3 μg/g), this value is consitent with that of another inner-city study, conducted in Baltimore, Maryland (0.18 μg/g) (Simons et al., 2007).

While many previous studies showed a consistent association between asthma and sensitization to allergens, the association between asthma and indoor environmental exposures is more complex (Arshad, 2010; Gaffin and Phipatanakul, 2009). A possible explanation for the inconsistent association for home environmental exposures may be preventive measures taken by the child's caretakers to reduce exposure to indoor allergens in response to a child's symptoms. The environmental sampling conducted for this study has some limitations, including that sampling indoor allergens at one point in time may not adequately represent long-term exposure to the allergen reservoir in the home. Climate factors such as humidity may promote dust mite growth (Institute of Medicine, 2000). Air sampling was conducted for a similar proportion of cases and controls during the same season to reduce potential bias from seasonal variation in allergen prevalence.

Allergen sensitization and indoor allergen exposure

This study found that children exposed to cockroach allergen at home were about six times more likely to be sensitized to cockroach allergen than children who were not exposed, in agreement with other studies examining this association. In the ICAS (Gruchalla et al., 2005), the relative risk of having a positive skin test for children exposed to cockroach allergen was 1.36 (95% CI: 1.24–1.48) compared to non-exposed children. Similarly, several other studies (Call et al., 1992; Eggleston et al. 1998; Huss et al., 2001; Sporik et al., 1990) also found that the prevalence of allergen-specific sensitization, measured by skin allergen testing, was significantly associated with a home's concentration of cockroach allergens. Unlike some of these studies, and possibly due to small sample sizes, we did not find a significant association between exposure and sensitization to any of the other allergens except for cockroach, although most ORs were elevated. Brussee et al. (2005) and Lindfors et al. (1999) found that dust mite and cat exposure during infancy were associated an increase in sensitization to these allergens by the age of 4 years. We found that a substantial proportion of the assessed individuals were sensitized to cat allergen (45.5%), dog allergen (54.2%) or dust mites (*Der f*: 50% and *Der p*: 55.7%) despite not being exposed to them in the home, suggesting other important sources of allergen exposure, such as at school or outdoors. Our study also found that use of a humidifier and having any pet in house were both associated with having four or more allergens/locations above their thresholds. This finding is plausible, as use of a humidifier would increase moisture in the home, which may promote an optimal environment for fungi and dust mite growth.

Sensitization and home exposure to allergens and asthma

The current study found that children both sensitized and exposed to cat allergen (but not other allergens) had a greater odds of prevalent asthma (OR = 7.08, 95% CI: 2.12–23.62) than those only sensitized (OR = 2.31, 95% CI: 1.01–5.32). Similar results were seen in a study by Gehring et al. (2001), where the greatest odds of wheezing and breathlessness were observed among those both exposed to and sensitized to cat allergen (OR = 14.24, 95% CI: 2.33–86.85) and dust mite (OR = 7.94, 95% CI: 1.08–58.11). In a cross-sectional study, Plaschke et al. (1999) showed that living with a cat aggravated symptoms and increased biomarkers of airway inflammation among asthmatics sensitized to cat or dog allergen. Two studies examining the joint effects of allergen sensitization and exposure found that children both exposed and sensitized to cockroach allergens had increased asthma symptoms and hospitalizations, but did not find similar results with other allergens (Gruchalla et al., 2005; Rosenstreich et al., 1997). We could not examine the joint effect of cockroach allergen exposure and sensitization on asthma status because cockroach levels at all case homes were below the detection limit.

Strengths and limitations

The current study is one of the few studies examining allergen sensitization and environmental exposures separately, their relationship to each other, as well as their joint association with asthma status. This study not only assessed multiple common indoor allergens, but also controlled for many potential confounders, including indoor and outdoor environmental factors. As with other case-control studies, a major concern was recall bias based on the possibility that cases may be more likely to recall exposures than equally exposed healthy controls. To reduce recall bias in the cross-sectional study, the cover letter for recruitment introduced the study as a general health-environment survey, rather than as an asthma survey, and all asthma-related questions were placed in the Part II the questionnaire only after socio-economic and environmental information was collected. Additionally, the responses to symptom questions from the cross-sectional questionnaire were compared with the face-to-face clinical interview, and high agreement rates were found, ranging from 80% to 100%. As the data on sensitization and home exposure were measured objectively through either skin allergen testing or home samples, recall or misclassification bias of the primary exposure does not pertain to this study.

The participation rate for the cross-sectional study (within which this investigation was conducted) was 43%. In order to address the possibility of selection bias, a short telephone interview was conducted with a random sample of the non-responders (N = 307, 23%). This follow-up interview included collection of basic demographics (e.g., child's age, gender, race/ethnicity, maternal educational level, and family income), the presence/absence of the seven criteria which had been used to identify asthma cases, and reasons for non-participation. The results showed that our initial study population may have under-represented African Americans in Buffalo, but there were no statistically significant differences between the respondents and non-respondents in terms of Hispanic proportion, gender, or age. The prevalence of various asthma symptoms was not significantly different between the respondents and non-respondents, which suggests there was no obvious selection bias resulting from differential study participation due to asthma status. The lower participation rate among African Americans may affect the representativeness of the study population with respect to the African American community and limit external validity, however, the influence of this limitation on the exposure-disease association should be minimal.

One limitation of our study is that the timing of introduction of allergen sources such as when pets were first brought into the home was unknown; therefore, the specific exposure window and its relationship with asthma could not be evaluated with our cross-sectional measurements. Another possible limitation of this study is that the number of cases and controls might be too small to achieve sufficient statistical power to detect small differences for most exposures, especially for the home environmental allergens and assessment of interactions between these exposures and sensitization. When the study power was computed, it was expected that an exposure rate of 30% or higher among the controls would be observed for an OR of 2.0. There was adequate power to detect a difference for sensitization to all allergens (all exposure rates >30%) and most indoor allergens, especially for cat allergen (96%, p = 0.10), except for cockroach and mouse, which had low exposure rates in most study homes. Though our multivariate analyses adjusted for family asthma history, residual confounding by genetics or confounding by other unknown or uncontrolled factors could have occurred.

Conclusion

This nested case-control study found significantly positive associations between asthma and sensitization to dust mite (*Der p* 1), cat, and dog allergens among children. The presence of cat allergen in a child's mattress was significantly associated with asthma status. We also found that children who were sensitized to cockroach were more likely to be living in a home with increased levels of cockroach allergen. The homes with pets and reported humidifier use were significantly associated with the presence of multiple indoor allergens above meaningful thresholds. Finally, compared to children without asthma, we found that asthmatic children were more likely to be sensitized and had significantly higher proportions of indoor exposure to cat allergens than those who were only sensitized or only exposed to cat allergens. This study supports the role of allergen exposure and sensitization in prevalent asthma, and suggests that the effect of allergen sensitization alone on asthma is more consistent than for environmental exposures, but their joint effect may be strongest. Further studies with larger sample sizes and enhanced methods to integrate multi-level environmental exposures are needed to confirm the findings of this study.

Appendix 1.

Allergen sampled	Sampling location for allergens		
	Kitchen	Family room	Bedroom
Dust mites (*Der f* 1 and *Der p* 1)		√	√
Cat		√	√
Dog		√	√
Cockroach (*Bla g* 1 and *Bla g* 2)	√	√	
Mouse	√		

A total of 9 allergens/locations sampled in the home.

References

Aligne, C.A., Auinger, P., Byrd, R.S., Weitzman, M.C., 2000. Risk factors for pediatric asthma contributions of poverty, race, and urban residence. Am. J. Respir. Crit. Care Med. 162 (3), 873–877.

Almqvist, C., Wickman, M., Perfetti, L., Berglind, N., Renstrom, A., Hedren, M., Larsson, L., Hedlin, G., Malmberg, P., 2001. Worsening of asthma in children allergic to cats, after indirect exposure to cat at school. Am. J. Respir. Crit. Care Med. 163, 694–698.

Almqvist, C., Li, Q., Britton, W.J., Kemp, A.S., Xuan, W., Tovey, E.R., Marks, G.B., CAPS Team, 2007. Early predictors for developing allergic disease and asthma: examining separate steps in the 'allergic march'. Clin. Exp. Allergy 37 (9), 1296–1302.

Arshad, S.H., 2010. Does exposure to indoor allergens contribute to the development of asthma and allergy? Curr. Allergy Asthma Res. 10, 49–55.

Asher, M.I., Keil, U., Anderson, H.R., Beasley, R., Crane, J., Martinez, F., Mitchell, E.A., Pearce, N., Sibbald, B., Stewart, A.W., Strachan, D., Weiland, S.K., Williams, H.C., 1995. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur. Respir. J. 8, 483–491.

Bloom, B., Dey, A.N., Freeman, G., 2006. Summary health statistics for U.S. children: National Health Interview Survey. Vital Health Stat. 10 (231).

Bloom, B., Cohen, R.A., 2007. Summary health statistics for U.S. children: National Health Interview Survey, 2006. Vital Health Stat. 10 (234).

Brussee, J.E., Smit, H.A., van Strein, R.T., Corver, K., Kerkhof, M., Wijga, A.H., Aalberse, R.C., Postma, D., Gerritsen, J., Grobbe, D.E., de Jongste, J.C., Brunekreef, B., 2005. Allergen exposure in infancy and the development of sensitization, wheeze, and asthma at 4 years. J. Allergy Clin. Immunol. 115, 946–952.

Byrd, R.S., Joad, J.P., 2006. Urban asthma. Curr. Opin. Pulm. Med. 12, 68–74.

Call, R.S., Smith, T.F., Morris, E., Chapman, M.D., Platts-Mills, T.A.E., 1992. Risk factors for asthma in inner city children. J. Pediatr. 21, 862–866.

Chew, G.L., 2009. Mite sensitization among Latina women in New York, where dust mite allergen levels are typically low. Indoor Air 19 (3), 193–197.

Crain, E.F., Weiss, K.B., Bijur, P.E., Hersh, M., Westbrook, L., Stein, R.E., 1994. An estimate of the prevalence of asthma and wheezing among inner-city children. Pediatrics 94, 356–362.

Dreborg, S., 1989. Skin tests used in type I allergy testing. Position paper. Allergy 44 (Suppl. 10).

Eggleston, P.A., Rosenstreich, D., Lynn, H., Gergen, P., Baker, D., Kattan, M., Mortimer, K.M., Mitchell, H., Ownby, D., Slavin, R., Malveaux, F., 1998. Relationship of indoor allergen exposure to skin test sensitivity in inner-city children with asthma. J. Allergy Clin. Immunol. 102, 4 (1), 563–570.

Gaffin, J.M., Phipatanakul, W., 2009. The role of indoor allergens in the development of asthma. Curr. Opin. Allergy Clin. Immunol. 9 (2), 128–135.

Gehring, U., Heinrich, J., Jacob, B., Richter, K., Fahlbusch, B., Schlenvoigt, G., Bischol, W., Wichmann, H-E., 2001. Respiratory symptoms in relation to indoor exposure to mite and cat allergens and endotoxins. Eur. Respir. J. 18, 555–583.

Gruchalla, R.S., Pongracic, J., Plaut, M., Evans III, R., Visness, C.M., Walter, M., Crain, E.F., Kattan, M., Morgan, W.J., Steinbach, S., Stout, J., Malindzak, G., Smartt, E., Mitchell, H., 2005. Inner City Asthma Study: relationships among sensitivity, allergen exposure, and asthma morbidity. J. Allergy Clin. Immunol. 115 (3), 478–485.

Huss, K., Adkinson Jr., N.F., Eggleston, P.A., Dawson, C., van Natta, M.L., Hamilton, R.G., 2001. House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program. J. Allergy Clin. Immunol. 107 (1), 48–54.

Institute of Medicine, 2000. Clearing the Air: Asthma and Indoor Air Exposures. National Academy Press, Washington, DC, p. 307.

Jaen, C.R., 1996. The Robert Wood Johnson Foundation Asthma Study. Progress report unpublished.

Jones, R., Lin, S., Munsie, J.P., Radigan, M., Hwang, S.A., 2008. Racial/ethnic differences in asthma-related emergency department visits and hospitalizations among children with wheeze in Buffalo, New York. J. Asthma 45, 916–922.

Kitch, B.T., Chew, G., Burge, H.A., Muilenberg, M.L., Weiss, S.T., Platts-Mills, T.A., O'Connor, G., Gold, D.R., 2000. Socioeconomic predictors of high allergen levels in homes in the greater Boston area. Environ. Health Perspect. 108 (4), 301–307.

Lau, S., Illi, S., Sommerfeld, S., Niggemann, B., Bergmann, R., von Mutius, E., Wahn, U., Multicentre Allergy Study Group, 2000. Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study. Lancet 356, 1392–1397.

Lin, S., Gomez, M.I., Hwang, S.A., Munsie, J.P., Fitzgerald, E.F., 2008. Self-reported home environmental risk factors for childhood asthma: a cross-sectional study of children in Buffalo, New York. J. Asthma 45, 325–332.

Lindfors, A., van Hage-Hamsten, M., Rietz, H., Wickman, M., Nordvall, S.L., 1999. Influence of interaction of environmental risk factors and sensitization in young asthmatic children. J. Allergy Clin. Immunol. 104 (1), 755–762.

Mannino, D.M., Homa, D.M., Pertowski, C.A., Ashizawa, A., Nixon, L.L., Johnson, C.A., Ball, L.B., Jack, E., Kang, D.S., 1998. Centers for Disease Control and Prevention. Surveillance for Asthma Prevalence—United States, 1960–1995. Morb. Mortal. Wkly. Rep. 47 (SS-1), 1–28.

Michel, O., Kips, J., Duchateau, J., Vertongen, F., Robert, L., Collet, H., Pauwels, R., Sergysels, R., 1996. Severity of asthma is related to endotoxin in house dust. Am. J. Respir. Crit. Care Med. 154, 6 (1), 1641–1646.

Moorman, J.E., Rudd, R.A., Johnson, C.A., King, M., Minor, P., Bailey, C., Scalia, M.R., Akinbami, L.J., 2007. National Surveillance for Asthma – United States, 1980–2004. MMWR Surveill. Summ. 19 56 (8), 1–54.

Paggiaro, P.L., Bacci, E., Amram, D.L., Rossi, O., Falini, D., 1986. Skin reactivity and specific IgE levels in the evaluation of allergic sensitivity to common allergens for epidemiological purposes. Clin. Allergy 6, 49–55.

Phipatanakul, W., Litonjua, A.A., Platts-Mills, T.A., Naccara, L.M., Celedón, J.C., Abdulkerim, H., Hoffman, E.B., Gold, D.R., 2007. Sensitization to mouse allergen and asthma and asthma morbidity among women in Boston. J. Allergy Clin. Immunol. 120 (4), 954–956.

Plaschke, P., Janson, C., Balder, B., Lowhagen, O., Jarvholm, B., 1999. Adult asthmatics sensitized to cats and dogs: symptoms, severity, and bronchial hyper-responsiveness in patients with furred animals at home and patients without these animals. Allergy 54, 843–850.

Platts-Mills, T.A., 1989. Dust mite allergen and asthma – a worldwide problem. J. Allergy Clin. Immunol. 83, 416.

Rosenstreich, D.L., Eggleston, P., Kattan, M., Baker, D., Slavin, R.G., Gergen, P., Mitchell, H., McNiff-Mortimer, K., Lynn, H., Ownby, D., Malveaux, F., 1997. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. N. Engl. J. Med. 336, 1356–1363.

Salome, C.M., Peat, J.K., Britton, W.J., Woolcock, A.J., 1987. Bronchial hyperresponsiveness in two populations of Australian schoolchildren. Relation to respiratory symptoms and diagnosed asthma. Clin. Allergy 17, 271–281.

Salo, P.M., Arbes, S.J., Crockett, P.W., Thorne, P.S., Cohn, R.D., Zeldin, D.C., 2008. Exposure to multiple indoor allergens in US homes and relationship to asthma. J. Allergy Clin. Immun. 121 (3), 678–684.

Salo, P.M., Jaramillo, R., Cohn, R.D., London, S.J., Zeldin, D.C., 2009. Exposure to mouse allergen in U.S. homes associated with asthma symptoms. Environ. Health Perspect. 117 (3), 387–391.

Sarpong, S.B., Karrison, T., 1997. Sensitization to indoor allergens and the risk for asthma hospitalization in children. Ann. Allergy Asthma Immunol. 79, 455–459.

Sarpong, S.B., Karrison, T., 1998. Skin test reactivity to indoor allergens as a marker of asthma severity in children with asthma. Ann. Allergy Asthma Immunol. 80, 303–308.

Sheehan, W.J., Rangsithienchai, P.A., Muilenberg, M.L., Rogers, C.A., Lane, J.P., Ghaemghami, J., Rivard, D.V., 2009. Mouse allergens in urban elementary schools and homes of children with asthma. Ann. Allergy Asthma Immunol. 102 (2), 125–130.

Simons, E., Curtain-Brosnan, J., Buckley, T., Breysse, P., Eggleston, P.A., 2007. Indoor environmental differences between inner city and suburban homes of children with asthma. J. Urban Health 84 (4), 577–590.

Sporik, R., Holgate, S.T., Platts-Mills, T.A.E., Cogswell, J.J., 1990. Exposure to house-dust mite allergen (*Der p*1) and the development of asthma in childhood: a prospective study. N. Engl. J. Med. 323, 502–507.

Squillace, S.P., Sporik, R.B., Rakes, G., Couture, N., Lawrence, A., Merriam, S., Zhang, J., Platts-Mills, T.A.E., 1997. Sensitization to dust mites as a dominant risk factor for adolescent asthma. Multiple regression analysis of a population-based study. Am. J. Respir. Crit. Care Med. 156, 1760–1764.

Surdu, S., Montonya, L.D., Tarbell, A., Carpenter, D.O., 2006. Childhood asthma and indoor allergens in native Americans in New York. Environ. Health 21, 5–22.

Wilson, N.W., Robinson, N.P., Hogan, M.B., 1999. Cockroach and other inhalant allergies in infantile asthma. Ann. Allergy Asthma Immunol. 83, 27–30.

Wong, G.W.K., Li, S.T., Hui, D.S.C., Fok, T.F., Zhong, N.S., Chen, Y.Z., Lai, C.K.W., 2002. Individual allergens as risk factors for asthma and bronchial hyperresponsiveness in Chinese children. Eur. Respir. J. 19, 288–293.